Remarks

Applicant has amended Claims 79-81, and Claims 32-56 are cancelled. Support for the claim amendments can be found throughout the specification, including, but not limited to, the following: Claim 79 in original claim 23 and on page 3, lines 21-26; Claim 80 on page 7, lines 29-31; and Claim 81 on page 13, line 23 through page 14, line 2. No new matter has been entered by the claim amendments and the Applicant respectfully request entry of the claim amendments.

Summary of Examiner's Interview conducted September 17, 2009

The Applicant graciously thanks the Examiner and Eric Winakur for conducting the Examiner's interview on September 17, 2009. The Applicant submitted a draft response differentiating the pending claims and the prior art references, Loeb and the Rameshraja et al. and discussed at length the differences between the disclosures of the blood substitutes in the prior art references and the pending claims. Mr. Winakur indicated that a specific scattering coefficient, between a range of 66%-5%, the size limitation of the blood substitute being about 80-5nm in size as to substantially reduce optical scattering, providing the wavelength of light is specific wavelength of 600-1500nm, and providing a certain amount or volume of the blood substitute to reduce optical scattering were differences not seen in the Loeb reference. The Applicant indicated that he would take Mr. Winakur's considerations into account in the response to the office action.

Claim Rejections - 35 USC § 102

I. Claims 1, 22, 63-71 & 79-81 rejected under 35 U.S.C. §102(b) as being anticipated by Loeb (U.S. Patent No. 4,448,188)

Claims 1, 79-81

The Examiner stated the following:

Loeb teaches a method for performing optical imaging [fiberoptic viewing system for sending a monochromatic light beam] (Col. 8, Line 47-54) or light based treatment [laser irradiation of the surface of the blood vessel for the removal of a plaque deposit] (Col. 3, Line 17-19) of at least a first tissue in an animal [blood vessel] (Abstract). Loeb teaches providing into the blood associated with first tissue a biologically effective amount of a low-scattering, oxygen-carrying blood substitute [substantially clear oxygen-bearing liquid] (Col. 4, Line 26-35). Loeb teaches wherein the low-scattering, oxygen-carrying blood substitute is selected to substantially reduce optical scattering [permit viewing with the blood vessel or use of the laser] (Col. 4, Line 22-25) from the blood fraction whilst substantially maintaining tissue oxygenation (Col. 3, Line

48-55). Loeb teaches applying an optical imaging or light-based treatment step to said at least a first tissue (Col. 3, Line 10-19).

The Applicant respectfully disagrees.

Loeb does not teach or suggest "a biologically effective amount of a low-scattering, oxygen-carrying blood substitute, wherein the low-scattering, oxygen-carrying blood substitute is selected to substantially reduce optical scattering", as to anticipate claim 1. The Examiner cites to the substantially clear oxygen-bearing liquid in Loeb, where substantially clear is to be understood that the transparency of the liquid or gas is sufficient to permit viewing within the blood vessel by use of a viewing system. Loeb, Col. 4, Lines 22-35, underlined added. In the field of optics, transparency is the physical property of allowing light to pass through a material, which allows much of the light that falls on the material to be transmitted, with little being reflected. However, scattering is a general physical process where light is forced to deviate from a straight trajectory by one or more localized non-uniformities in the medium through which light passes, and includes deviation of reflected radiation from the angle predicted by the law of reflection. As such, a material that is transparent may not necessarily be non-scattering.

Most importantly, Loeb teaches and enables that the oxygen-bearing liquid is a perfluorocarbon (PFC) emulsion. While PFC emulsions are transparent, PFC emulsions are not effective at reducing attenuation or reduce scattering, because the solution contains micron-scale particles that will scatter light similar to red blood cells. See Villard et al. thesis at 36-37, Villard '2001, cited in IDS and in Office Action dated November 17, 2008. Moreover, the present application states that PFC's are unsuitable for use in the present invention because PFC's cause significant light scattering due to the size of PFC's being sufficiently close to the wavelengths of light used in imaging and light therapy (600-1500 nm). Present Application, Pages 23, line 30-Page 24, line 5. The inventors even validated that PFC's are unsuitable for use in the present invention due to their scattering properties. *Id.* As such, the substantially clear/ transparent oxygen-bearing liquid in Loeb does not teach or suggest a low-scattering, oxygen-carrying blood substitute, wherein the low-scattering, oxygen-carrying blood substitute is selected to substantially reduce optical scattering. Therefore, the rejection of Claim 1 under §102(b) is improper and respectfully requested to be withdrawn.

Regarding Claim 79, Loeb does not teach or suggest "low-scattering, oxygen-carrying blood substitute reduces the scattering coefficient of the blood associated with said at least a first tissue to about one half of the scattering coefficient of whole blood or less at a sample

wavelength of between about 600 nm and about 1500 nm", as to render Claim 79 anticipated. Loeb is silent to scattering coefficients, and as indicated above, Loeb's blood substitute highly scatters light. As such, the §102(b) rejection of Claim 79 is respectfully requested to be withdrawn, accordingly.

Regarding Claim 80, Loeb does not teach or suggest the "low scattering, oxygen carrying blood substitute includes a size less than about 80 nm", as to render Claim 80 anticipated. Loeb is silent as to the size of the oxygen carrying blood substitute, and more so, Loeb teaches PFC's, which include particles of about 200 nanometers. Present Application, page 23, line 30-page 24, line 5. As such, the §102(b) rejection of Claim 80 is respectfully requested to be withdrawn, accordingly.

Regarding Claim 81, Loeb does not teach or suggest "the biologically effective amount results in a reduced scattering coefficient of whole blood to about 66% to 5%", as to render Claim 81 anticipated. Loeb is silent to scattering coefficients, and as indicated above, Loeb's blood substitute highly scatters light, let alone to be enabled to reduce the scattering coefficient of whole blood to a particular percentage. As such, the §102(b) rejection of Claim 81 is respectfully requested to be withdrawn, accordingly.

Claim 22

The Examiner stated that "Loeb teaches a blood substitute wherein the largest species in said solution in a size of about 6 nanometers (Col. 5, Line 61 -63 & Col. 6, Line 27-30). The Applicant respectfully disagrees, as Loeb only discloses that the PFC emulsion be prepared with a particle size below about 0.1 micrometers. Loeb, Col. 5, lines 61-63. First, 0.1 micrometers is not about 6 nanometers. Second, PFC's are generally known to be within the range of about 200 nanometers (Present Application, Pages 23, line 30- Page 24, line 5); where 200 nanometers is not 6 nanometers. Thus, Loeb fails to teach or disclose each and every limitation of Claim 22, and the Applicant respectfully requests the Examiner to withdraw the rejection accordingly.

Claims 63-71

Regarding Claims 63-71, these claims are further believed allowable over Loeb for the same reasons set forth with respect to parent Claim 1 and since each dependent claim sets forth additional elements that are not disclosed in Loeb. Applicant asserts that the rejection of Claims 63-71 under 35 U.S.C. §102(b) has been overcome and should be withdrawn. Notice to that effect is requested.

II. Claims 2-21, 23-31, 57-62, 72-74 & 76-78 rejected under 35 U.S.C. §103(a) as being unpatentable over Loeb (U.S. Patent No. 4,448,188) as applied to claim 1 , 22,63- 71 & 79-81 above, and further in view of Rameshraja et al., Current aspects in pharmacology of modified hemoglobins, Advanced Drug Delivery Reviews, Volume 40, Issue 3, Blood Substitutes, 28 February 2000, Pages 185-198

Claims 2-5

The Examiner stated the following:

Loeb teaches the hemoglobin solution contained human hemoglobin (Col. 4, Line 54) and teaches using perfluorocarbons as a blood substitute, but fails to teach a blood substitute with modified hemoglobins (Col. 5, Line 13-33). However, Rameshraja teaches that two types of blood substitutes are in advance stages of development: perfluorocarbons (PFC) and modified hemoglobins. Rameshraja teaches PFCs have disadvantages such as inherent immunological response and higher risk to develop infection (Page 186, 1. Introduction) and many new developments regarding modified hemoglobin have been done to improve its physiological properties. Rameshraja teaches a blood substitute which comprises human hemoglobin (Page 193, Part 2.7). Rameshraja teaches a blood substitute which is substantially non-particulate, acellular, bovine hemoglobin solution [Oxyglobin] (Page 187, Part 2 & Page 192, Part 2.6) which allows for improved oxygen metabolism at the cellular level (Page 192, 2.6). It would have been obvious to one of ordinary skill in the art to substitute the blood substitute of Loeb with the Oxyglobin as taught by Rameshraja in order to have improved oxygen metabolism at the cellular level (Page 192, 2.6)

The Applicant respectfully disagrees and traverses the rejection herewith.

Rameshraja states that "Biopure in 1998 received the clearance from Food and Drug Administration (FDA) to market the first ever 'blood substitute' Oxyglobin™ (HBOC-301, hemoglobin glutamer-200(bovine)) for the treatment of anemia in dogs. Rameshraja, Page 192, Part 2.6, Col. 1. HBOC-301 is not further mentioned or discussed in Rameshraja. Rameshraja states that HBOC-201 may allow for improved oxygen metabolism at the cellular level, and that (HBOC-201) is a glutaraldehyde polymerized bovine hemoglobin. Rameshraja, Page 192, Part 2.6, Col. 1-Col. 2. Therefore, it would not have been obvious to one of ordinary skill in the art to substitute the blood substitute of Loeb with the Oxyglobin as taught by Rameshraja in order to have improved oxygen metabolism at the cellular level, because Rameshraja does not state that Oxyglobin improves oxygen metabolism at the cellular level. As such, the Examiner's §103(a) rejection is legally inappropriate and the Applicant respectfully requests the Examiner to withdraw the §103(a) rejection accordingly.

Claims 6-10

Regarding Claims 6-10, these claims are further believed allowable over Loeb in view of Rameshraja for the same reasons set forth with respect to parent Claim 1 and since each dependent claim sets forth additional elements that are not disclosed in Loeb in view of Rameshraja. Applicant asserts that the rejection of Claim 6-10 under 35 U.S.C. §103(a) has been overcome and should be withdrawn. Notice to that effect is requested.

Claims 11-21 & 31

Regarding Claims 11-21 and 31, these claims are further believed allowable over Loeb in view of Rameshraja for the same reasons set forth with respect to parent Claim 1 and since each dependent claim sets forth additional elements that are not disclosed in Loeb in view of Rameshraja. Applicant asserts that the rejection of Claim 11-21 and 31 under 35 U.S.C. §103(a) has been overcome and should be withdrawn. Notice to that effect is requested.

More so, regarding Claim 20, Loeb in view of Rameshraja does not teach or suggest "low-scattering, oxygen-carrying blood substitute reduces the hematocrit of the blood associated with said at least a first tissue to an amount effective to result in a half maximal or lower scattering coefficient μ_s' according to the equation $\mu_{tot}' = \mu_a + \mu_s'$, where μ_a is the absorption coefficient and μ_{tot}' is the total attenuation coefficient". As such, the Examiner's §103(a) rejection of Claim 20 is legally insufficient, and the Applicant respectfully requests the Examiner to withdraw the rejection accordingly.

Claims 23-30

Regarding Claims 23-30, these claims are further believed allowable over Loeb in view of Rameshraja for the same reasons set forth with respect to parent Claim 1 and since each dependent claim sets forth additional elements that are not disclosed in Loeb in view of Rameshraja. Applicant asserts that the rejection of Claim 23-30 under 35 U.S.C. §103(a) has been overcome and should be withdrawn. Notice to that effect is requested.

More so, regarding Claim 23, Loeb does not teach or suggest "low-scattering, oxygen-carrying blood substitute reduces the scattering coefficient of the blood associated with said at least a first tissue to about one half of the scattering coefficient of whole blood or less at a sample wavelength of between about 600 nm and about 1500 nm", as to render Claim 23 obvious. As indicated above, optical transparency and optical scattering are two different optical properties of light, and any blood substitute disclosed by Loeb does not reduce optical scattering,

let alone reducing the scattering coefficient of the blood associate with said at least a first tissue to about one half the scattering coefficient of whole blood at a sample wavelength of between about 600 and about 1500 nm. As such, the Examiner's rejection of Claim 23 is legally inappropriate and the Applicatn respectfully requests the Examiner to withdraw the rejection accordingly.

Claims 57-62 & 72-74

Regarding Claims 57-62 and 72-74, these claims are further believed allowable over Loeb in view of Rameshraja for the same reasons set forth with respect to parent Claim 1 and since each dependent claim sets forth additional elements that are not disclosed in Loeb in view of Rameshraja. Applicant asserts that the rejection of Claim 57-62 and 72-74 under 35 U.S.C. §103(a) has been overcome and should be withdrawn. Notice to that effect is requested.

Claims 76-78

Regarding Claims 76-78, these claims are further believed allowable over Loeb in view of Rameshraja for the same reasons set forth with respect to parent Claim 1 and since each dependent claim sets forth additional elements that are not disclosed in Loeb in view of Rameshraja. Applicant asserts that the rejection of Claim 76-78 under 35 U.S.C. §103(a) has been overcome and should be withdrawn. Notice to that effect is requested.

Examiner's Response to Arguments filed February 17, 2009

The Examiner stated the following:

Loeb teaches the blood substitute to be substantially clear to allow for optical viewing or use of a laser. Also Loeb teaches a method for maximizing for the desired transparency to a particular laser wavelength (Col. 4, Line 43-46). Rameshraja teaches using a blood substitute [Oxyglobin@] with physical properties (Page 192, Part 2.6) that are inherent to the blood substitute as disclosed with the Applicant's Specification (Page 24-25)...While Applicant directs claims to certain observable properties when low-scattering, blood substitute is infused into the patient in the manner disclosed, the measured properties as claimed are inherent results. Applicant's description on page 29 gives evidence to the inherent properties.

The Applicant respectfully disagrees and traverses the rejection herewith.

The Examiner is inappropriately using Applicant's own invention to show that Oxyglobin includes inherent properties of "the low-scattering, oxygen carrying blood substitute is selected to substantially reduce optical scattering from the blood fraction whilst substantially maintaining tissue oxygenation". No where in the prior art references, Examiner's reasoning or rationale, is there shown or provided that Oxyglobin would have or result in the low-scattering, oxygen carrying blood substitute is selected to substantially reduce optical scattering from the blood

fraction whilst substantially maintaining tissue oxygenation. The Examiner cites to Example 1 of the present application, where the inventors determined the effect of OCT signal attenuation at a wavelength of 1310nm due to blood in the murine Right Ventricle (RV), dilutions were placed between two glass slides separated by a 0.15 mm air space. The inventors selected a 0.15 mm distance as a compromise between obtaining sufficient signal amplitude from the lower surface at high hematocrit (e.g., 45%) and a measurable attenuation at low hematocrit (e.g., 5%). The inventors recorded OCT images through the sample dilutions prepared at the same hematocrits as above, i.e., 40, 30, 20, 10, 8, 5, and 3%. The results indicated to the inventors that the scattering properties of whole murine blood decreased from 1.801 +/- 0.245 to 0.253 +/- 0.176 1/mm ($p<0.05$) when the hematocrit was reduced from physiological levels to <5%. No where is it shown in the prior art references or by the Examiner's rationale that Oxyglobin would include decreased scattering properties from 1.801 +/- 0.245 to 0.253 +/- 0.176 1/mm ($p<0.05$) when the hematocrit was reduced from physiological levels to <5% by placing dilutions of blood to hematocrits of 40, 30, 20, 10, 8, 5, and 3% between two glass slides separated by a 0.15 mm air space and detecting OCT signal attenuation at 1310 nm due to blood in the murine Right Ventricle (RV). Again, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993).

More so, Example 1 in the present application clearly shows that the "low-scattering, oxygen carrying blood substitute is selected to substantially reduce optical scattering from the blood fraction whilst substantially maintaining tissue oxygenation" is an unobvious difference in the prior art. The Examiner indicated that the burden is shifted to the applicants to prove that the subject matter to be shown in the prior art does not possess the characteristic relied on". *In re Fitzgerald*, 619 F.2d 70, 205 USPQ 596 (CCPA 1980). Using Oxyglobin to show decreased scattering properties from 1.801 +/- 0.245 to 0.253 +/- 0.176 1/mm ($p<0.05$) when the hematocrit was reduced from physiological levels to <5% by placing dilutions of blood to hematocrits of 40, 30, 20, 10, 8, 5, and 3% between two glass slides separated by a 0.15 mm air space and detecting OCT signal attenuation at 1310 nm due to blood in the murine Right Ventricle (RV) clearly shows that one of ordinary skill in the art would not use Oxyglobin in such manner, steps, or preparation to show a low-scattering, oxygen carrying blood substitute is selected to substantially reduce optical scattering from the blood fraction whilst substantially maintaining tissue

oxygenation. As such, the steps of substantially reducing optical scattering from the blood fraction whilst substantially maintaining tissue oxygenation is an unobvious difference in the prior art and any rationale provided by the Examiner.

Finally, the Examiner is reminded that the pending claims are method or process claims and not claiming the product itself. The Examiner stated the following:

Products of identical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

Claim 1 claims the "method for performing optical imaging or light-based treatment of at least a first tissue...providing into the blood associated with at least a first tissue a biologically effective amount of a low-scattering, oxygen-carrying blood substitute, wherein the low-scattering, oxygen-carrying blood substitute is selected to substantially reduce optical scattering from the blood fraction whilst substantially maintaining tissue oxygenation...". Under the principles of inherency, if a prior art device, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art device. When the prior art device is the same as a device described in the specification for carrying out the claimed method, it can be assumed the device will inherently perform the claimed process. *See* MPEP §2112.02, citing *In re King,* 801 F.2d 1324, 231 USPQ 136 (Fed. Cir. 1986). There is no evidence in Loeb or Rameshraja that Oxyglobin would include the steps of performing optical imaging or light-based treatment of at least a first tissue, providing into the blood associate with at least a first tissue a biologically effective amount of low scatting, oxygen carrying blood substitute, wherein the low-scatting, oxygen blood substitute is **selected** to substantially reduce optical scattering from the blood fraction whilst substantially maintaining tissue oxygenation. There is no selection process in Loeb or Rameshraja for substantially reducing optical scattering. As such, the Examiner has inappropriately applied the legal standard inherency for apparatus claims against the pending method claims, and the Applicant respectfully requests the Examiner to withdraw the rejection accordingly.

III. Claims 75 & 82 rejected under 35 U .S.C. §103(a) as being unpatentable over Loeb (US Patent No. 4,448,188) as applied to claims 1 , 22, 63-71 & 79-81 above, and further in view of Swanson et al. (US Patent No. 5,321,501).

The Examiner stated the following:

Loeb teaches using a fiberoptic viewing system (Col. 8, Line 46-54) but fails to teach optical coherence tomography. However, Swanson teaches optical coherence tomography

(Figure 1 B & Claim 2) for producing cross-sectional images (Col. 4, Line 59-63) with sharp focus and sensitivity (Col. 2, Line 24-33). It would have been obvious to one of ordinary skill in the art to modify the method of Loeb to include the optical coherence tomography imaging as taught by Swanson in order to produce cross-sectional images (Col. 4, Line 59-63) with sharp focus and sensitivity (Col. 2, Line 24-33).

The Applicant respectfully disagrees. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 409, 82 USPQ2d 1385, 1396 (2007). There is no showing or enablement that one of ordinary skill in the art would be able to modify the fiberoptic viewing system in Loeb with the OCT system as taught by Swanson. The fiberoptic viewing system includes means for supplying viewing light through the distal end 24 of the conduit 22, which can be accomplished by transmitting a light through the fiberoptic viewing bundle 28 or as shown in FIG. 2, by providing a separate light transmitting bundle 48; and the use of a separate light transmitting bundle is preferred for sending a monochromatic light beam through the fiberoptic viewing bundle 28. Loeb, Col. 8, lines 47-54. However, Swanson's Figure 1B teaches an optical frequency domain reflectometer utilizing a spectrally coherent optical source 79 which is frequency modulatable in the form of a linear FM chirp by signal generator 78; the output from source 79 passes to a sample assembly 28 and to a reference mirror 44; since changes in optical path length are not being utilized for this embodiment to perform longitudinal scanning, the remainder of the reference assembly shown in FIG. 1A is not required nor are modulators 34, 38 and 40; and a lens such as lens 36 may or may not be required. Such features and limitations of Swanson's OCT system render any combination with Loeb's fiberoptic viewing system questionable and inoperable, as Swanson's OCT system requires substantially different optical components and parameters that one of ordinary skill in the art would not be able to modify the method of Loeb for cross-sectional images with sharp focus and sensitivity. For at least these reasons, the Applicant submits that the §103(a) rejection of the claims is inappropriate, and respectfully requests the Examiner to withdraw the §103(a) rejection accordingly.

More so, Claims 75 and 82 are further believed allowable over Loeb in view of Swanson for the same reasons set forth with respect to Claim 1 indicated above, and since each dependent claim sets forth additional elements that are not disclosed in Loeb in view of Swanson. Applicant asserts that the rejection of Claim 75 and 82 under 35 U.S.C. §103(a) has been overcome and should be withdrawn. Notice to that effect is requested.

Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of the application, the Examiner is invited to telephone the undersigned at the number provided below.

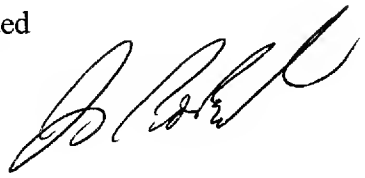
Any remarks in support of patentability of one claim should not be imputed to any claim, even if similar terminology is used. Additionally, any remarks referring to only a portion of a claim should not be understood to base patentability on that portion; rather, patentability must rest on each claim taken as a whole. Applicants respectfully traverse each of the Examiner's rejections and each of the Examiner's assertion regarding what the prior art shows or teaches, even if not expressly discussed herein. Although amendments have been made, no acquiescence or estoppel is or should be implied thereby. Rather, the amendments are made only to expedite prosecution of the present application, and without prejudice to presentation or assertion, in the future, of claims on the subject matter affected thereby.

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicants reserve the right pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child, or related prosecution history shall not reasonably infer that Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

The Applicant submits payment of a one month extension fee herewith. No additional fees are believed due with the filing of this document. However, in the event the U.S. Patent and Trademark Office determines that other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such

petitions and/or other fees due in connection with the filing of this documents to Deposit Account No. 18-2000, of which the undersigned is an authorized signatory.

Respectfully submitted



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October 5, 2009

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